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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,986	10/18/2001	Larry Gold	NEX01/C8	1060
25871	7590	01/16/2004	EXAMINER	
SWANSON & BRATSCHE L.L.C.			FORMAN, BETTY J	
1745 SHEA CENTER DRIVE			ART UNIT	
SUITE 330			PAPER NUMBER	
HIGHLANDS RANCH, CO 80129			1634	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,986	GOLD ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2 and 4-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2 and 4-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>2/02</u> . | 6) <input type="checkbox"/> Other: _____ |

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FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 31 October 2003 in which claims 2 and 4 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 1 July 2003 under 35 U.S.C. 112, second paragraph are withdrawn in view of the amendments. All other rejections are maintained as reiterated below.

The arguments have been thoroughly reviewed and are discussed below.

The examiner for this application has changed. Please address future correspondence to Examiner BJ Forman, Art Unit: 1634.

Claims 2 and 4-8 are under prosecution.

Application status

2. The present application is a continuation of multiple ancestral applications dating back to the filing of serial no. 07/71 4, 1 31, June 10, 1991. However, for prosecution the claims are given the effective filing date of the amendment in which they were presented, February 1 3, 2002, because the subject matter is not supported by the disclosure for the reasons set forth herein.

Response to Arguments

Applicant states that the instant specification is identical to the specification of parent application 07/714,131. Applicant argues that because the instant specification supports the instant claims, the claims are entitled to the effective filing date of the '131 application. The argument has been considered but is not found persuasive for the reasons discussed in detail below regarding the New Matter rejection.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2 and 4-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for identifying or assisting in identifying the binding site or regulatory region of a nucleic acid binding protein by competing a nucleic acid ligand to a nucleic acid binding protein with DNA or RNA of the binding site region and determining whether the ligand blocks the binding protein from binding to the binding site region thereby assisting in the identification of the DNA or RNA regulatory region. In a passage cited by applicant in support of the claimed subject matter, the specification mentions that the SELEX

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method can be used "to assist in the identification and characterization of any binding protein site for DNA or RNA", noting that "binding sites function in transcriptional or translational regulation of gene expression" (page B4, line 33-page 55, line 1). In a further cited portion of the specification, proteins known to bind nucleic acids, e.g., polymerases and noncatalytic proteins are mentioned as leading via the SELEX method to "high affinity RNA ligands that bind to the active site of the protein" (page 57, lines 20-25).

Finally, in Example 2, also cited by applicant, the ability of a nucleic acid ligand to HIV reverse transcriptase (RT) to inhibit RT activity was tested by competing the ligand with the "starting population", i.e., the candidate mixture of nucleic acids, from which it was concluded that the ligand "either blocks or directly interacts with the catalytic site of the enzyme" (page 81 , lines 20-31). In addition to lack of competition with the binding region, it is the enzyme active site which is assessed, not the binding site. Another passage in the specification describes determination of the minimal size of the translational operator, the RNA sequence to which phage -1-4 DNA polymerase (gp 43) binds. In this experiment the minimal size of the operator was determined by analysis of gp43 binding to hydrolysis fragments of the operator and sequence determinations were made by assessing binding of gp 43 to operator sequences mutated in the hairpin or loop regions. It was concluded that binding of gp 43 and its transcriptase activity reside in distinct regions of the operator sequence (page 66, lines 1 5-34). Thus, nowhere in the specification is the claimed method for identifying the binding site of a nucleic acid binding protein via competition with binding region DNA or RNA described. It is suggested that claim 1 might be rewritten according to disclosed methods with the caveat that the patentable utility of a method appearing to serve only for further research would be doubtful.

Response to Arguments

5. Applicant points to page 62, line 32 through page 63, line 8 for support for the instant claims. As Applicant acknowledges, the cited passage describes ligands that inhibit the function of binding proteins to bind to nucleic acids. The passages follows:

The methods of the present invention are useful for obtaining nucleic acids which will inhibit function of a target protein, and are particularly useful for obtaining nucleic acids ligands which inhibit the function of proteins whose function involves binding to nucleic acids . . .

Applicant's citation is acknowledged. However, the instant claims are drawn to a method for "identifying a....binding site". While the cited passage broadly describes inhibition of ligands resulting from binding between ligands and nucleic acid-binding proteins, the cited passage does not teach or describe the instantly claimed identification of a binding site.

Applicant argues that the passage on page 65, line 35-page 69, line 33 teaches ligand binding to and inhibition of a DNA/RNA binding protein which "**can** be useful in identifying the binding site of the DNA/RNA, because the inhibitory ligand's sequence **can** be similar to that of the binding site on the wild type mRNA." The cited passage, as highlighted above, merely suggests that the ligands could be useful for identifying a binding site but does not teach the instantly claimed identification of a binding site.

Applicant further argues that Example 2 "illustrates how a ligand that binds to a binding site of an RNA binding protein **can** have sequence and/or structure that is informative about the binding site on the RNA (in this case, tRNA)." However, again the cited passage merely suggests applications but does not teach the instantly claimed identification of a binding site.

Applicant's cited passages do not illustrate that the specification, as originally filed, supports the instantly claimed method for identifying a binding site. The rejection is maintained.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 2, 3 and 5-8 rejected under 35 U.S.C. 102(b) as being anticipated by Giordano et al. (5,859,227).

Regarding claim 2, the patent discloses the claimed method comprising (a) providing an RNA molecule that interacts with an RNA binding protein, i.e., an RNA ligand to a binding protein (column 11, lines 61-64); (b) contacting the RNA ligand with a mixture of the RNA binding protein and RNA binding region subfragments (column 11, lines 41-43); (c) determining binding protein binding to RNA binding region subfragments and determining the nucleotide sequence of the regulatory region (column 11, line 64-column 12, line 1).

Regarding claim 3, the embodiment wherein the RNA binding molecule has a similar structure to the RNA binding region subfragments is disclosed (column 11, lines 23-25).

Regarding claims 5-8, the embodiments wherein the RNA binding region is a promoter, an ORI, et al., wherein the protein regulates transcription or translation, and wherein the protein is a transcriptional activator or repressor, a promoter complex member or a translational repressor are disclosed (column 3, lines 1-11) .

8. Claims 2, 3, 5, 6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by the patent to Weissman et al, (5,861 ,246).

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Regarding claim 2, the patent discloses the claimed method as follows: the octamer DNA nucleotide sequence, wt-oct, was known to bind the transcription factor, OctT3, (column 9, lines 22-39) such that the DNA qualifies as the nucleic acid of step (a) in the claim. In step (b), the ligand, wt-oct, was contacted with a mixture of DNA binding site regions, BS03/9 and BS08, and the DNA binding protein, OctT3 as (wt-oct-oct-r3 complex) (column 9, lines 40-66). The step (c) determination found that the ligand did not block the protein from binding and one of the binding regions, the BS08 sequence, was the optimal binding sequence for the OctT3 protein (column 9, line 66-column 10, line 3).

Regarding claim 3, the embodiment wherein the ligand and the binding region are similar in structure is disclosed in the competitive binding experiments (column 9, lines 40-64).

Regarding claim 5, the embodiment wherein the DNA binding site region is a promoter is disclosed in the patent (column 6, lines 1 1-1 9).

Regarding claims 6 and 8, the embodiment wherein the protein regulates transcription is disclosed in the patent (column 2, lines 60-62).

Claim Rejections - 35 USC § 102/103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 4 is rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Weissman et al. (5,861,246).

The patent discloses claim 2 from which claim 4 depends as set forth above at paragraph 5 and further discloses a method for providing a nucleic acid ligand to a DNA binding protein which is essentially the same as that of claim 4 (column 4, lines 36-50). It is not clear in the patent whether the DNA ligand to the DNA binding protein, wt-oct, was obtained by this method. However, if it was not so obtained, it would have been obvious to the skilled practitioner in the art at the time the claimed invention was made to use the disclosed method in view of the patent demonstration of its efficacy for providing RNA molecules that bind RNA binding proteins. The skilled practitioner would have been motivated further by his/her obvious familiarity with the routinely practiced SELEX method which was essentially the same as the disclosed method and was well established in the art as the method of choice for obtaining nucleic acids that bind proteins.

Response to Arguments

11. Applicant argues that the above rejections under 35 U.S.C. 102 (b) and under 35 U.S.C. 102(b)/103 are improper because the effective filing date of the instant claims is earlier than the filing dates of the cited references. The argument has been considered but is not found

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persuasive because, as state above, the effective filing date for the instant claims is February 13, 2002. Therefore, the cited references qualify as prior art. The rejections are maintained.

12. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878 until 13 January 2004. Starting 14 January 2004, the examiner's phone number will be (517) 272-0741. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196. Starting 14 January 2003, the receptionist telephone number will be (517)-272-0507.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
January 13, 2004